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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/480,389	01/11/2000	Bruce M. Boman	CATX-N	4258

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EXAMINER
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HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 09/480,389	<b>Applicant(s)</b> BOMAN, BRUCE M.	
	<b>Examiner</b> Anne Holleran	<b>Art Unit</b> 1643	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 18 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☒ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 24-28,32-35,37-44,55-57 and 59-72.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
 12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_  
 13. ☐ Other: \_\_\_\_\_.

Continuation of 3. NOTE: The amendment to claim 24, introducing the phrase "wherein said disease or said disease susceptibility trait is one in which at least about 10% of affected individuals have a germline mutation in one of two or more subject genes" raises a new issue under 35 U.S.C., 112, 2nd because the preamble of the method is now not in accordance with the end result of the claimed method. This phrase also raises an issue under new matter, because the limitation of affecting "at least about 10% of individuals" having a disease or disease susceptibility trait is introduced and described in the specification with respect to colorectal cancer only. Because the specification teaches that the claimed immunoassays are intended for the purpose of detecting disease or disease susceptibility associated with a germline mutation in one or both alleles of a subject gene (page 5, lines 30-32), the introduction of the limitation that said disease or said disease susceptibility trait is one in which at least about 10% of affected individuals have a germline mutation in one of two or more subject genes appears to be a change in scope from what was originally contemplated. On pages 7-8, the specification provides a list of diseases, but fails to indicate that these diseases are contemplated because they have the criterion of being a disease or disease susceptibility trait that is one in which at least about 10% of affected individuals have a germline mutation in one or two or more subject genes. Therefore, the teachings with respect to colorectal cancer do not appear to be representative of all of the diseases originally intended to be encompassed by the claimed inventions, and the introduction of the new limitation appears to be directed to carving out a new genus that was not originally contemplated.

The introduction of the phrase "where each of said subject genes is known to have said germline mutation in individuals affected with said disease or disease susceptibility trait" raises a new issue under 35 U.S.C., 112, 1st for lack of written description, because the specification fails to identify the criteria of "knowing". This rejection would be a reinstatement of a rejection that was earlier made on similar grounds in the Office action mailed 7/14/2004. Furthermore, the introduction of this phrase raises a new issue under 35 U.S.C. 112, 2<sup>nd</sup> because it apparently contradicts the preamble "wherein said disease or said disease susceptibility trait is one in which at least about 10% of affected individuals have a germline mutation. The contradiction arises because in part of the claim there is a range of diseased individuals that possibly have a germline mutation (i.e. at least about 10% of affected individuals), but in the second part of the claim, it appears that all diseased individuals have a germline mutation (i.e. each of said subject genes is known to have said germline mutation in individuals affected with said disease or disease susceptibility trait).

Continuation of 5. Applicant's reply has overcome the following rejection(s): Rejection of claims 24-28, 32-35, 37-44, 55-57 and 59-72 under 35 U.S.C. 112, first as failing to comply with the written description requirement would be overcome by this amendment, if entered, because the amendment removes that phrase "wherein said disease or said disease susceptibility trait has been associated with a germline mutation...".

Continuation of 7. Response to arguments against rejection of claims 24-28, 32-35, 43, 44, 55-57 and 61 under 35 U.S.C. 103(a). This rejection is maintained because the after-final amendment will not be entered. Applicant argues that the claimed inventions are not obvious over Pece in view of Nozawa, because Pece's ratios are not the same as the ratios calculated in the claimed inventions. Applicant asserts that because of the phrase "wherein each of the said subject genes has been associated with such a disease or such a disease susceptibility trait" (version of claim 24 before after-final amendment, at lines 10-11), the ratios of the claimed inventions differ from Pece's ratios, because not all of Pece's subject genes are "disease associated". This is not found persuasive because the phrase "associated with a disease" may be broadly interpreted. In the case of Pece, a ratio is made of endoglin expression to alpha-v/beta-5 integrin expression. The argument could be made that both of these genes are "disease associated", because a mutation in endoglin is known to occur in a "vascular disorder"; and alpha-V/beta-5 integrin is also associated with vascular disorders, such as angiogenesis. Therefore, the rejection is maintained.

*Am Harris*  
ALANA M. HARRIS, PH.D.  
PRIMARY EXAMINER  
08/01/2005